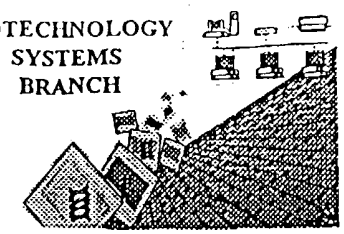
BIOTECHNOLOGY
SYSTEMS
BRANCH



RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/722,903
Source: IFW0
Date Processed by STIC: 8/19/04

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.2 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm> , **EFS Submission User Manual** - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 06/05/04):** U.S. Patent and Trademark Office, 220 20th Street S., Customer Window, Mail Stop Sequence, Crystal Plaza Two, Lobby, Room 1B03, Arlington, VA 22202

Revised 05/17/04

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 10/722,903

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1	Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
2	Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.
3	Misaligned Amino Numbering	The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
4	Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
5	Variable Length	Sequence(s)____contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
6	PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
7	Skipped Sequences (OLD RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES " response to include the skipped sequences
8	Skipped Sequences (NEW RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence <210> sequence id number <400> sequence id number 000
9	Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents
10	Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
11	Use of <220>	Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
12	PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
13	Misuse of n/Xaa	"n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid

IFWO

RAW SEQUENCE LISTING DATE: 08/19/2004
PATENT APPLICATION: **US/10/722,903** TIME: 10:59:18

Input Set : **A:\GTC-53_Sequence Listing.txt**
Output Set: **N:\CRF4\08192004\J722903.raw**

Does Not Comply
Corrected Diskette Needed
(pg. 2-4)

<110> APPLICANT: GTC Biotherapeutics, Inc.
<120> TITLE OF INVENTION: Modified Antibodies Stably Produced in Milk and Methods of Producing Same
<130> FILE REFERENCE: GTC-53
<140> CURRENT APPLICATION NUMBER: 10/722,903
<141> CURRENT FILING DATE: 2003-11-26
<150> PRIOR APPLICATION NUMBER: US 60/429,606
<151> PRIOR FILING DATE: 2002-11-27
<160> NUMBER OF SEQ ID NOS: 11
<170> SOFTWARE: PatentIn version 3.2
<210> SEQ ID NO: 1
<211> LENGTH: 2028
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Human Ig germline H-chain G-E-A region B: gamma-4 constant region, 3' end
<400> SEQUENCE: 1

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gcaggtggcg ccagccaggt gcacacccaa tgcccatgag cccagacact ggaccctgca 120
tggaccatcg cggatagaca agaaccgagg ggcctctgcg ccctgggccc agctctgtcc 180
cacaccgcgg tcacatggca ccacctctct tgcagcttcc accaagggcc catccgtctt 240
ccccctggcg ccctgctcca ggagcacctc cgagagcaca gccgccctgg gctgcctggt 300
caaggactac ttccccgaac cggtgacggt gtcgtggaac tcaggcgccc tgaccagcgg 360
cgtgcacacc ttcccggctg tcctacagtc ctcaggactc tactccctca gcagcgtggt 420
gaccgtgccc tccagcagct tgggcacgaa gacctacacc tgcaacgtag atcacaagcc 480
cagcaacacc aaggtggaca agagagttgg tgagaggcca gcacagggag ggagggtgtc 540
tgctggaagc caggctcagc cctcctgcct ggacgcaccc cggctgtgca gccccagccc 600
agggcagcaa ggcatgcccc atctgtctcc tcacccggag gcctctgacc accccactca 660
tgctcaggga gagggtcttc tggatttttc caccaggctc ccggcaccac aggctggatg 720
cccctacccc aggccctgcg catacagggc aggtgctgcg ctcagacctg ccaagagcca 780
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gtccaaatat ggtcccccat gcccatcatg cccaggtaag ccaacccagg cctcgccctc 960
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gtgctgacgc atccacctcc atctcttcct cagcacctga gttcctgggg ggaccatcag 1080
tcttcctgtt ccccccaaaa cccaaggaca ctctcatgat ctcccggacc cctgaggtca 1140
cgtgcgtggt ggtggacgtg agccaggaag accccgaggt ccagttcaac tggtacgtgg 1200
atggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagttc aacagcacgt 1260
accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaacggc aaggagtaca 1320
agtgcaaggt ctccaacaaa ggcctcccgt cctccatcga gaaaaccatc tccaaagcca 1380
aaggtgggac ccacggggtg cgagggccac acggacagag gccagctcgg cccaccctct 1440

RAW SEQUENCE LISTING DATE: 08/19/2004
PATENT APPLICATION: **US/10/722,903** TIME: 10:59:18

Input Set : **A:\GTC-53_Sequence Listing.txt**
Output Set: **N:\CRF4\08192004\J722903.raw**

80 gccctgggag tgaccgctgt gccaacctct gtccctacag ggcagccccg agagccacag 1500
82 gtgtacaccc tgcccccatc ccaggaggag atgaccaaga accaggtcag cctgacctgc 1560
84 ctggtcaaag gcttctaccc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 1620
86 gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1680
88 agcaggctaa ccgtggacaa gagcaggtgg caggagggga atgtcttctc atgctccgtg 1740
90 atgcatgagg ctctgcacaa ccactacaca cagaagagcc tctccctgtc tctgggtaaa 1800
92 tgagtgccag ggccggcaag cccccgctcc ccgggctctc ggggtcgcgc gaggatgctt 1860
94 ggcacgtacc ccgtctacat acttcccagg cacccagcat ggaaataaag cacccaccac 1920
96 tgccctgggc ccctgtgaga ctgtgatggt tctttccacg ggtcaggccg agtctgaggc 1980
98 ctgagtgaca tgagggaggc agagcgggtc ccactgtccc cacactgg 2028

101 <210> SEQ ID NO: 2
102 <211> LENGTH: 61
103 <212> TYPE: DNA
104 <213> ORGANISM: Homo sapiens
107 <220> FEATURE:
108 <221> NAME/KEY: misc_feature
109 <223> OTHER INFORMATION: IgG4 Hinge Region Nucleic Acid
111 <400> SEQUENCE: 2
112 tctgcagagt ccaaatatgg tcccccatgc ccatcatgcc caggtaagcc aacccaggcc 60
114 t 61

117 <210> SEQ ID NO: 3
118 <211> LENGTH: 12
119 <212> TYPE: PRT
120 <213> ORGANISM: Homo sapiens
123 <220> FEATURE:
124 <221> NAME/KEY: misc_feature
125 <223> OTHER INFORMATION: IgG4 Hinge Region Amino Acid
127 <400> SEQUENCE: 3
129 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
130 1 5 10

133 <210> SEQ ID NO: 4
134 <211> LENGTH: 33
135 <212> TYPE: DNA
136 <213> ORGANISM: oligonucleotide
139 <220> FEATURE:
140 <221> NAME/KEY: misc_feature
141 <223> OTHER INFORMATION: S241P Oligo Nucleic Acid
143 <400> SEQUENCE: 4
144 ggtcccccat gtcctccctg cccaggtaag cca 33

147 <210> SEQ ID NO: 5
148 <211> LENGTH: 11
149 <212> TYPE: PRT
150 <213> ORGANISM: oligonucleotide
153 <220> FEATURE:
154 <221> NAME/KEY: misc_feature
155 <223> OTHER INFORMATION: S241P Oligo Amino Acid
157 <400> SEQUENCE: 5
159 Gly Pro Pro Cys Pro Pro Cys Pro Gly Lys Pro
160 1 5 10

Insert in section <220> - <223>, Invalid Response

Insert in section <220> - <223>, Invalid Response

Pls see item #10 on error summary sheet.

<Mandatory> <213> Responses has to be either artificial/Unknown or genus/species.

RAW SEQUENCE LISTING DATE: 08/19/2004
PATENT APPLICATION: **US/10/722,903** TIME: 10:59:18

Input Set : **A:\GTC-53_Sequence Listing.txt**
Output Set: **N:\CRF4\08192004\J722903.raw**

```
163 <210> SEQ ID NO: 6
164 <211> LENGTH: 65
165 <212> TYPE: DNA
166 <213> ORGANISM: Homo sapiens
169 <220> FEATURE:
170 <221> NAME/KEY: misc_feature
171 <223> OTHER INFORMATION: IgG4 Hinge Region Nucleic Acid
173 <400> SEQUENCE: 6
174 cttctctctg cagagtccaa atatggtccc ccatgcccat catgcccagg tccgccaacc     60
176 caggc                                                                65
179 <210> SEQ ID NO: 7
180 <211> LENGTH: 12
181 <212> TYPE: PRT
182 <213> ORGANISM: Homo sapiens
185 <220> FEATURE:
186 <221> NAME/KEY: misc_feature
187 <223> OTHER INFORMATION: IgG4 Hinge Region Amino Acid
189 <400> SEQUENCE: 7
191 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
192 1               5                   10
195 <210> SEQ ID NO: 8
196 <211> LENGTH: 65
197 <212> TYPE: DNA
198 <213> ORGANISM: Homo sapiens
201 <220> FEATURE:
202 <221> NAME/KEY: misc_feature
203 <223> OTHER INFORMATION: IgG2 Hinge Region Nucleic Acid
205 <400> SEQUENCE: 8
206 cttctctctg cagagcgcaa atgttgtgtc gagtgcccac cgtgcccagg tccgccaacc     60
208 caggc                                                                65
211 <210> SEQ ID NO: 9
212 <211> LENGTH: 12
213 <212> TYPE: PRT
214 <213> ORGANISM: Homo sapiens
217 <220> FEATURE:
218 <221> NAME/KEY: misc_feature
219 <223> OTHER INFORMATION: IgG2 Hinge Region Amino Acid
221 <400> SEQUENCE: 9
223 Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
224 1               5                   10
227 <210> SEQ ID NO: 10
228 <211> LENGTH: 33
229 <212> TYPE: DNA
230 <213> ORGANISM: oligonucleotide
233 <220> FEATURE:
234 <221> NAME/KEY: misc_feature
235 <223> OTHER INFORMATION: Oligo 2014 Nucleic Acid
237 <400> SEQUENCE: 10
238 gaggagcagt tccagtctac ttaccgagtg gtc                                  33
```

same error

RAW SEQUENCE LISTING DATE: 08/19/2004
PATENT APPLICATION: **US/10/722,903** TIME: 10:59:18

Input Set : **A:\GTC-53_Sequence Listing.txt**
Output Set: **N:\CRF4\08192004\J722903.raw**

241 <210> SEQ ID NO: 11
242 <211> LENGTH: 11
243 <212> TYPE: PRT
244 <213> ORGANISM: oligonucleotide — same error
247 <220> FEATURE:
248 <221> NAME/KEY: misc_feature
249 <223> OTHER INFORMATION: Oligo 2014 Amino Acid
251 <400> SEQUENCE: 11
253 Glu Glu Gln Phe Gln Ser Thr Tyr Arg Val Val
254 1 5 10

VERIFICATION SUMMARY DATE: 08/19/2004
PATENT APPLICATION: **US/10/722,903** TIME: 10:59:19

Input Set : **A:\GTC-53_Sequence Listing.txt**
Output Set: **N:\CRF4\08192004\J722903.raw**